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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,950	03/19/2004	Christine Konradi	04843/120003	8080

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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
07/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/804,950	KONRADI ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 39-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 4/07/2009.

2. Currently Claims 1-2 and 39-41 are pending. Claims 3-38 have been cancelled.

3. The following rejections are newly applied as necessitated by amendment.

4. This action is FINAL.

Interview Summary

5. Applicant's summary of the interview on 3/11/2009 is acknowledged (p. 4 2nd paragraph).

Withdrawn Rejections

6. The rejection of the claims under 35 USC 102 made in section 10 of the previous office action (1/08/2009) is moot based upon amendments to the claims.

7. The rejection of the claims under 35 USC 103(a) as obvious over Seitink et al. made in section 12 of the previous office action (1/08/2009) is moot based upon amendments to the claims and consideration of the arguments made in the reply.

Claim Objections

8. Claim 2 is objected to because the claim specifically recites nonelected subject matter. The Claims require the analysis of the non-elected nucleic acid molecules.

Applicant has elected for examination of the claim in so far as it requires ATP Synthase, F1 complex, 0 subunit; ATP Synthase, F0 complex, d subunit; ATP Synthase, F0 complex, C3 subunit; ATP Synthase, F1 complex, gamma polypeptide 1; ATP Synthase F0 complex subunit F in the reply to restriction (4/20/2006). Prior to allowance of this, the non-elected subject matter will be required to be deleted from the claim.

Response to Arguments

The reply request that the objection to Claim 2 be held in abeyance until consideration of the generic Claim 1 is given (p. 5 1st paragraph).

The claim objection will be maintained until Claim 1 is in condition for allowance or until the claim has been amended to reflect only the elected nucleic acid molecules.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van den Heuvel et al. (American Journal Human Genetics 1998 Vol 62 p. 262) in view of Lockhart et al. (US Patent 6040138 March 21, 2000).

With regard to Claim 1, Van den Heuvel et al. teaches a mutation in the human nuclear gene encoding the AQDQ subunit of the mitochondrial respiratory chain complex I (abstract). Van den Heuvel et al discloses the cDNA sequences of the nuclear gene which results in the mutation (p. 263 1st column 3rd paragraph). Therefore Van den Heuvel et al. teaches nucleic acids molecules which encode the polypeptides of complex I of the mitochondrial respiratory chain being naturally coded for by a nuclear gene. Van den Heuvel et al. teaches the use of only nuclear genes to detect a pathogenic mutation in a population which caused enzyme deficiency (p. 262 1st column 1st paragraph).

However Van den Heuvel et al. does not teach placing the nucleic acid fragments of the mutation onto a microarray.

With regard to Claim 1, Lockhart et al. teaches placing oligonucleotides probes onto an array (solid support) to detect expression (Abstract).

With regard to Claim 39, Lockhart et al. teaches the probes can be at least 40

nucleotides in length (column 15 lines 53-60).

With regard to Claims 40-41, Lockhart et al. teaches that the array of probes can comprise up to 100 different oligonucleotide probes (abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to bind the nuclear gene associated with the mutations taught by Van den Heuvel to the array taught by Lockhart et al. with a reasonable expectation of success. The ordinary artisan would want to incorporate the nuclear gene associated with mutations onto the array because Lockhart et al. teaches that probes on an array can be used to detect a large number of different target nucleic acids at once and determine the relative abundance of each in a sample (Column 2 lines 35-55). Therefore the ordinary artisan would be motivated have an array consisting of only the nuclear gene associated with the mutation taught by Van den Heuvel in order to detect the mutation in a number of patients simultaneously.

12. Claims 1-2, 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US Patent Application Publication US 2006/0099578 May 11, 2006) as evidenced by Wallace (US Patent 5494794 February 27, 1996, referred to as Wallace '794) in view of Van den Heuvel and Smeitink (Bioessays 2001 VOl. 23 p. 518) and Papaconstantinou et al. (US Patent Application publication 2008/0187911 August 7, 2008 priority to 1/30/2003).

With regard to Claim 1, Wallace et al. teaches microarray consisting of probes for mitochondrial genes (abstract). Wallace et al. teaches that these arrays can contain

subsets of probes drawn to mitochondrial energy (p. 2 paragraph 10). Wallace et al. teaches that the microarray can be composed of mtDNA genes from NADH, Cytochrome b, Cytochrome c, ATP synthase 6, ATP synthase 8 (Table 1 and p. 3 paragraph 17). Therefore Wallace et al. teaches a microarray comprising nucleic acid molecules that encode polypeptides of complex I, II, III, IV, or V (e.g. NADH, Cytochrome b, Cytochrome c, ATP synthase 6, ATP synthase 8). Wallace et al. teaches that the arrays can be designed such that genes related to OXPHOS are detected (p. 9 paragraph 64).

OXPHOS is composed of 5 enzyme complexes assembled from 13 mitochondrial DNA and 50 nuclear DNA subunits (as evidenced by Wallace '794 Column 1 lines 60-67). Wallace '794 teaches that OXPHOS is composed of Complex I (NADH); complex III (cytochrome c and cytochrome b); Complex IV (cytochrome c, COI, COII, COIII); and complex V (ATP synthase) (as evidenced by Wallace '794 Column 1 lines 60-67 and Column 2 lines 1-5). Therefore an array related to OXPHOS would include nucleic acid molecules of mitochondrial respiratory chain of complex I, III, IV, and V.

With regard to Claim 2, Wallace et al. teaches the array can include any number of genes related to mitochondrial function including ATP Synthase, F1 complex, 0 subunit; ATP Synthase, F0 complex, d subunit; ATP Synthase, F0 complex, C3 subunit; ATP Synthase, F1 complex, gamma polypeptide 1; ATP Synthase F0 complex subunit F (Table 3).

With regard to Claim 39, Wallace et al. teaches that the probes are 20-30 nucleotides in length (p. 4 paragraph 24).

With regard to Claims 40-41, Wallace et al. teaches the microarray can contain probes for all genes involved in mitochondrial biology or can contain probes for at least 10 genes or at least 25 genes (p. 6 paragraph 42).

However, Wallace et al. does not teach a microarray which consists of only nucleic genes of the mitochondrial respiratory chain.

With regard to Claim 1, Van den Heuvel and Smeitink teach although deficiencies can be either the mitochondrial DNA or nuclear DNA, the percentage of those patients with mitochondrial DNA abnormalities is relatively low (p. 518 2nd column 1st full paragraph). Van den Heuvel and Smeitink teaches that therefore screening for common mtDNA mutations in patients with established OXPHOS disorder (ATP through oxidative phosphorylation) is unsatisfactory (p. 518 2nd column 1st full paragraph). Therefore Van den Heuvel and Smeitink teach that it would be useful to screen for abnormalities in nuclear DNA.

Papaconstantinou et al. teaches microarrays of nucleic encoded genes (paragraph 120 p. 20). Papaconstantinou et al. teaches that the microarray for detection of a particular invention can be composes solely of gene of nuclear origin wherein the genes encoded by the mitochondrial DNA were removed (paragraph 126 p. 24). Therefore Papaconstantinou et al. teaches that micorarrays can be designed such that only nuclear genes are detected.

Therefore it would be prima facie obvious to one of ordinary skill in the art to modify the various subsets of microarrays taught by Wallace et al. to design an array consisting of at least 90% nuclear genes for the use of detection of nuclear

abnormalities as taught by Van den Heuvel and Smeitink. The ordinary artisan would be motivated to design an array of only nuclear genes because Van den Heuvel and Smeitink teach that the vast majority of abnormalities are from nuclear DNA. Further Papaconstantinou et al. teaches that that the ordinary artisan would be able to design microarrays consisting only of nuclear genes. It would have been obvious to one of ordinary skill in the art at the time the invention was made to design an array only of nuclear genes with a predictable expectation of successful screening of diseases associated with nuclear genes. The ordinary artisan would be motivated to produce an array consisting of only nuclear genes because Van den Heuvel and Smeitink teach that the majority of mutations are associated with nuclear genes.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday-Friday 8AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634

/Sarae Bausch/
Primary Examiner, Art Unit 1634